AMENDMENTS TO THE CLAIMS

1. Cancelled

2. (Currently Amended) A pharmaceutical composition for topical administration to treat recurrent herpes infections consisting essentially of a synergistic combination of an active ~~topically acceptable~~ antiviral ingredient ~~substance~~ selected from the group consisting of foscarnet, acyclovir, ~~cidofovir, descielovir, famcielovir, ganciclovir, lobucavir,~~ penciclovir, ~~PMEA, valacyclovir, 2242, PAA, PFA~~ and 9-[4-hydroxy-2-(hydroxymethyl)butyl]guanine (H2G) or an ~~ester,~~ salt ~~or solvate~~ thereof and an active anti-inflammatory glucocorticoid ingredient selected from the group consisting of ~~alclometasone, amicinonide, beclomethasone, budesonide, ciclesonide, clobetasone, clocortolone, cloprednol, cortison, desonide, desoximethasone, dexamethasone, diflorosane, diflucortolone, difluprednate, fludrocortisone, fludroxycortid, flumethasone, flunisolide, fluocinolone acetonide, fluocinonide, fluocortin, fluocortolone, flupredniden, fluticasone, halcinonide, halobetasol, halometasone,~~ hydrocortisone, ~~methylprednisolone, mometasone, paramethasone, prednisolone, prednicarbate, prednisone, prednylidene, rofleponide, tipredane and triamcinolone~~ and ~~their~~ esters thereof, ~~salts and solvates~~ in a pharmaceutically acceptable carrier, wherein said synergistic combination of antiviral and glucocorticoid is more effective than either component alone.

3. Cancelled

4. (Currently Amended) The pharmaceutical composition according to claim 2, wherein the anti-inflammatory glucocorticoid is ~~selected from the group consisting of~~ hydrocortisone, ~~alclometasone, desonide, flupredniden, flumethasone, hydrocortisone butyrate, clobetasone, triamcinolone acetonide, betamethasone, budesonide, desoximethasone, diflorosane, flucinolone, fluocortolone, fluticasone, methylprednisolone aceponate, mometasone and rofleponide or an ester, salt or solvate thereof~~.

5. (Currently Amended) The pharmaceutical composition according to claim 2, wherein the anti-viral ~~substance~~ is foscarnet and the anti-inflammatory glucocorticoid is hydrocortisone~~, or an ester thereof~~.

6. Cancelled

7. (Currently Amended) ~~The~~ A pharmaceutical composition according to claim 2, wherein the antiviral ~~substance~~ is acyclovir~~, or an ester, salt or solvate thereof,~~ and the anti-inflammatory glucocorticoid is hydrocortisone~~, or an ester thereof~~.

8. (Currently Amended) The pharmaceutical composition according to claim 5 ~~comprising~~ wherein said foscarnet is contained in an amount of 0.1-10% (w/w) ~~foscarnet~~ and said hydrocortisone is contained in an amount of 0.005-3% (w/w) ~~hydrocortisone~~.

9. (Currently Amended) The pharmaceutical composition according to claim 8 ~~comprising~~wherein said foscarnet is contained in an amount of 1-5% (w/w) ~~foscarnet~~.

10. (Currently Amended) The pharmaceutical composition according to claim 8 ~~comprising~~ wherein said foscarnet is contained in an amount of 0.3-3% (w/w) ~~foscarnet~~ and said hydrocortisone is contained in an amount of 0.25-1% (w/w) ~~hydrocortisone~~.

11. Cancelled

12. Cancelled

13. (Currently Amended) The pharmaceutical composition according to claim 7 ~~comprising~~wherein said acyclovir is contained in an amount of 0.1-10% (w/w) ~~acyclovir~~ and said hydrocortisone is contained in an amount of 0.005-3% (w/w) ~~hydrocortisone~~.

14. (Currently Amended) The pharmaceutical composition according to claim 13 ~~comprising~~ wherein said acyclovir is contained in an amount of 1-5% (w/w) ~~acyclovir~~.

15. (Currently Amended) The pharmaceutical composition according to claim 14 ~~comprising~~ wherein said hydrocortisone is contained in an amount of 0.25-1% (w/w) ~~hydrocortisone~~.

16. (Currently Amended) A cream, lotion, gel, ointment, plaster, stick or pen containing a pharmaceutical composition according to any one of claims 2, 4, 5, 7-10 and 13-15.

17. Cancelled

18. (Currently Amended) A method for treating recurrent herpes virus infections of the skin or mucous membranes in mammals having or identified as being at risk of developing said infections comprising topically administering thereto, in combination or in sequence, a therapeutically synergistic dose of an active ~~topically acceptable~~ antiviral ~~substance~~ ingredient selected from the group consisting of foscarnet, acyclovir, ~~cidofovir, desciclovir, famciclovir, gancielovir, lobucavir,~~ penciclovir~~, PMEA, valacyclovir, 2242, PAA, PFA~~ and 9-[4-hydroxy-2-(hydroxymethyl)butyl]guanine (H2G) or ~~an ester~~, salt ~~or solvate~~ thereof and an active anti-inflammatory glucocorticoid ingredient selected from the group consisting of ~~alclometasone, amicinonide, beclomethasone, budesonide, ciclesonide, clobetasone, clocortolone, cloprednol, cortison, desonide, desoximethasone, dexamethasone, diflorosane, diflucortolone, difluprednate, fludrocortisone, fludroxycortid, flumethasone, flunisolide, fluocinolone acetonide, fluocinonide, fluocortin, fluocortolone, fluprednidene, fluticasone, halcinonide, halobetasol, halometasone,~~ hydrocortisone~~, methylprednisolone, mometasone, paramethasone, prednisolone, prednicarbate, prednisone, prednylidene, rofleponide, tipredane and triamcinolone~~ and ~~their~~ esters thereof, ~~salts and solvates~~ in a pharmaceutically acceptable carrier, wherein said synergistic dose of antiviral and glucocorticoid is more effective than either component used alone.

19. Cancelled

20. (Currently Amended) The method according to claim 18, wherein the anti-inflammatory glucocorticoid is ~~selected from the group consisting of~~ hydrocortisone~~, alclometasone, desonide, flupednidene, flumethasone, hydrocortisone butyrate, clobetasone, triamcinolone acetonide, betamethasone, budesonide, desoximethasone, diflorosane, flucinolone, fluocortolone, fluticasone, methylprednisolone aceponate, mometasone and rofleponide or an ester, salt or solvate thereof~~.

21. (Previously Presented) The method according to claim 18, wherein the antiviral substance is foscarnet and the anti-inflammatory glucocorticoid is hydrocortisone, or an ester thereof.

22. Cancelled

23. (Currently Amended) A method according to claim 18, wherein the antiviral substance is acyclovir, or ~~an ester,~~ salt ~~or solvate~~ thereof, and the anti-inflammatory glucocorticoid is hydrocortisone, or an ester thereof.

24. (Currently Amended) A method for treating recurrent herpes virus infections of the skin or mucous membranes in mammals having or identified as being at risk of developing said infections comprising topically administering thereto a therapeutic dose of a topically acceptable composition according to any one of claims 2, 4, 5, 7-10 and 13~~4~~-15.

25. (Previously Presented) The method according to claim 24 wherein the composition is contained in a cream, lotion, gel, ointment, plaster, stick or pen.

26. Cancelled

27. (Currently Amended) A method according to any one of claims 18, 20, 21 and ~~20~~-23, wherein the antiviral substance and the glucocorticoid are administered 1 to 10 times per day.

28. (Previously Presented) The method according to claim 27, wherein the antiviral substance and the glucocorticoid are administered 3 to 4 times per day.

29. (Currently Amended) The method according to claim 40~~26~~, wherein the antiviral substance and the glucocorticoid are administered 1 to 10 times per day.

30. (Previously Presented) The method according to claim 29, wherein the antiviral substance and the glucocorticoid are administered 3 to 4 times per day.

31. (Currently Amended) A method according to any one of claims 18, 20, 21 and ~~20~~-23 wherein the antiviral substance and the glucocorticoid are administered in combination and are contained in a cream, lotion, gel, ointment, plaster, stick or pen.

32. Cancelled

33. (Previously Presented) The method according to claim 24, wherein the antiviral substance and the glucocorticoid are administered 1 to 10 times per day.

34. (Previously Presented) The method according to claim 33, wherein the antiviral substance and the glucocorticoid are administered 3 to 4 times per day.

35. (Previously Presented) The method according to claim 31, wherein the antiviral substance and the glucocorticoid are administered 1 to 10 times per day.

36. (Previously Presented) The method according to claim 35, wherein the antiviral substance and the glucocorticoid are administered 3 to 4 times per day.

37. Cancelled

38. Cancelled

39. Cancelled

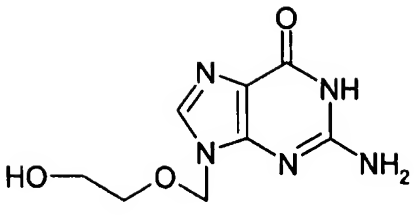
40. (Previously Presented) The method according to claim 18, wherein said antiviral is acyclovir and said anti-inflammatory glucocorticoid is hydrocortisone~~, or an ester thereof~~.

In this Supplemental Amendment, submitted for the sole purpose of expediting prosecution and without disclaimer of unclaimed subject matter, Applicants have restricted the claims to specific antiviral substances and particular glucocorticoids. Applicants have also amended the claims to better define the term "synergistic." In support of "synergistic combination" and "synergistic dose," Applicants offer the following comments.

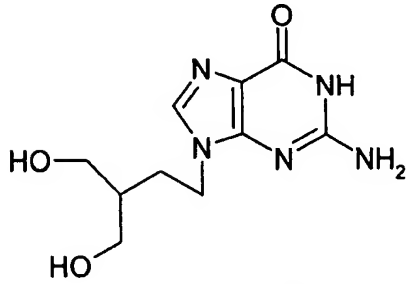
Applicants have submitted a manuscript entitled "ME-609: A treatment for recurrent herpes simplex virus infections" which summarizes the preclinical and early clinical experience of ME-609, a composition containing 5% acyclovir and 1% hydrocortisone. As discussed on pages 14-18 and in Table 2, the combination of acyclovir and hydrocortisone showed improved efficacy as compared to acyclovir or hydrocortisone alone. The Harmenberg et al. (2003, *Antiviral Chemistry & Chemotherapy* 14:205-215) and Evans et al. (2002, *Antimicrobial Agents and Chemotherapy* 46:1870-1874) references reiterate these results.

The results obtained for the acyclovir and hydrocortisone combination are similar to those reported for the combination of foscarnet and hydrocortisone (*see* Harmenberg et al. manuscript page 15, lines 21-22 and page 18, lines 3-5 as well as the instant Specification, Tables 2-4 and Figure 3).

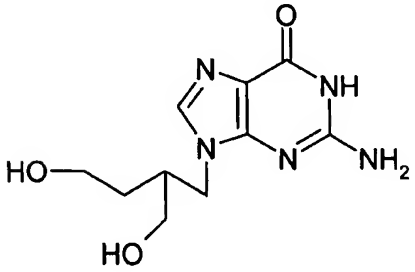
Applicants note that acyclovir, penciclovir and H2G (i.e. 9-[4-hydroxy-2-(hydroxymethyl)butyl]guanine) have a very close structural and functional resemblance as shown below.



acyclovir



penciclovir



9-(4-hydroxy-2-(hydroxymethyl)butyl)guanine

Based the close structural and functional similarity between acyclovir, penciclovir and H2G, penciclovir and H2G are fully expected to have an efficacy similar to that of acyclovir when used as a treatment for herpes simplex virus infections. As a matter of interest, Applicants point out that 9-[4-hydroxy-2-(hydroxymethyl)butyl]guanine has the trivial name of "H2G," but has recently been awarded the official INN (international non-proprietary nomenclature) name "omaciclovir."

Similarly, hydrocortisone and its esters are closely related both structurally and functionally and are thus fully expected to perform similarly.

Rejections Under 35 U.S.C. § 103

The Examiner rejected claims 1-4, 7, 13-21 and 23-40 as obvious over Levin (USP 5,656,301), claims 1-5, 7-10, 13-21 and 23-40 as obvious over Smith (USP 4,902,678) in view of Underwood (USP 3,317,384) and claims 6, 11, 12 and 22 as being obvious over Smith in combination with Underwood and Chemical Abstract 103:172328.